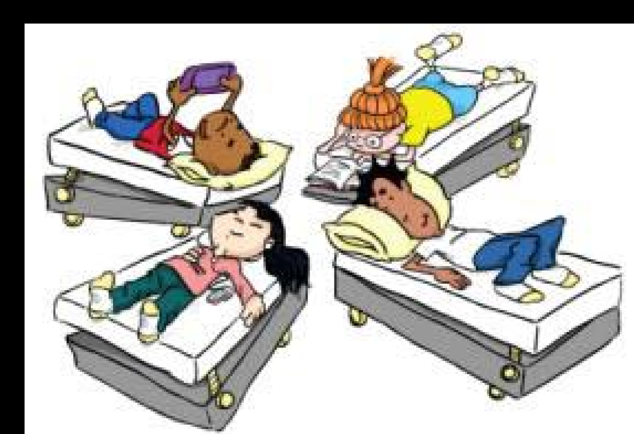
Intake of Fish and Omega-3 (n-3) Fatty Acids: Effect on Humans during Actual and Simulated Weightlessness

S.M. Smith,[1] D.L. Pierson,[1] S.K. Mehta,[2] S.R. Zwart[3]

[1]NASA Johnson Space Center, [2]Enterprise Advisory Services, Inc., [3]Universities Space Research Association

Abstract

Space flight has many negative effects on human physiology, including bone and muscle loss. Bone and muscle are two systems that are positively affected by dietary intake of fish and n-3 fatty acids. The mechanism is likely to be related to inhibition by n-3 fatty acids of inflammatory cytokines (such as TNFα) and thus inhibition of downstream NF-κB activation. We have documented this effect in a 3-dimensional cell culture model, where NF-κB activation in osteoclasts was inhibited by eicosapentaenoic acid, an n-3 fatty acid. We have also indentified that NF-κB activation in peripheral blood mononuclear cells of Space Shuttle crews. We found that after Shuttle flights of ~2 wk, expression of the protein p65 (evidence of NF-κB activation) was increased at landing ($P < 0.001$). When evaluating the effects of n-3 fatty acid intake on bone breakdown after 60 d of bed rest (a weightlessness analog). We found that after 60 d of bed rest, greater intake of n-3 fatty acids was associated with less N-telopeptide excretion (Pearson $r = –0.62$, $P < 0.05$). We also evaluated the relationship of fish intake and bone loss in astronauts after 4 to 6 mo missions on the International Space Station. Higher consumption of fish during flight was associated with higher bone mineral density (Pearson $r = –0.46$, $P < 0.05$). Together, these findings provide evidence of the cellular mechanism by which n-3 fatty acids can inhibit bone loss, and preliminary human evidence of the potential for n-3 fatty acids to counteract bone loss associated with space flight. This study was supported by the NASA Human Research Program.

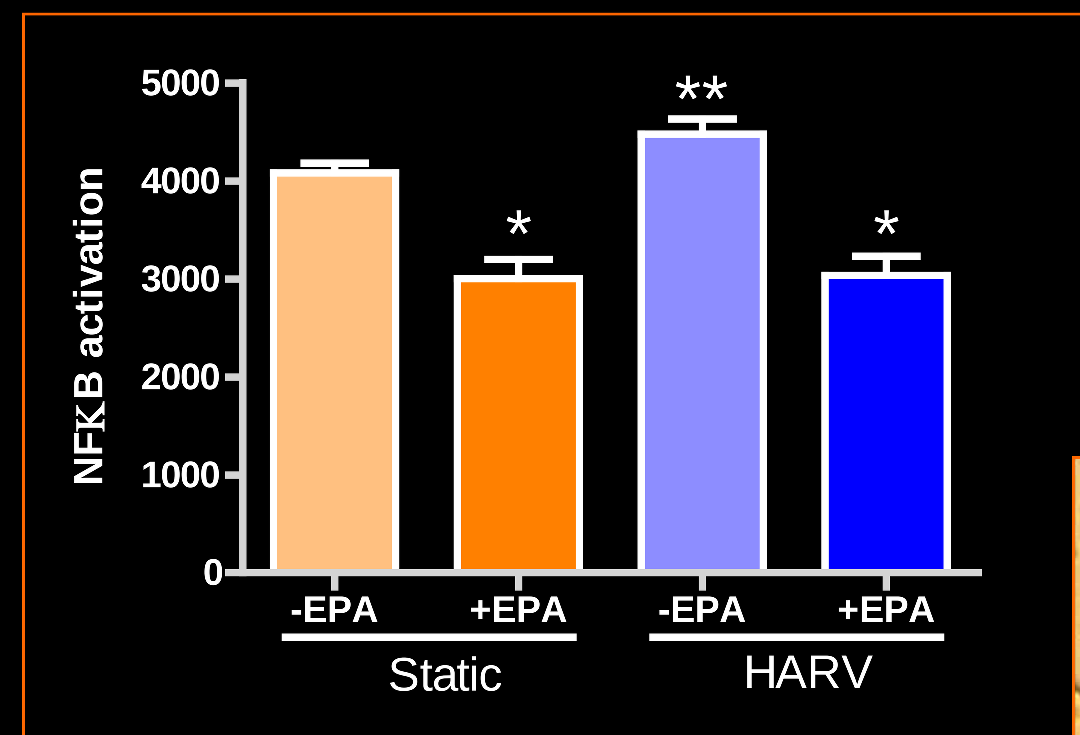


Methods

Several models were studied:

1. Cell culture studies examining the effects of an omega-3 fatty acid addition on osteoclast activation and NFκB activation.
2. Studies of NFκB activation in astronauts before and after short-duration Space Shuttle missions
3. Bed rest studies examining differences in intake of omega-3 fatty acids and relationship to bone resorption
4. ISS studies of reported fish intake related tot postflight bone loss.

These studies and details of the methods used have been described in published in greater detail (Zwart et al., 2010).



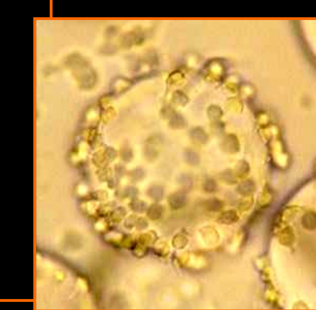


Figure 1. NF-kB activation in differentiated RAW264.7 cells after 24 h of exposure to modeled weightlessness in a rotating high aspect ratio vessel (HARV) or static control with or without an earlier 24-h incubation with eicosapentaenoic acid (EPA). Different symbols represent statistically significant differences between groups. The effect of the HARV ($p < 0.05$) and EPA ($p < 0.001$) were significant.

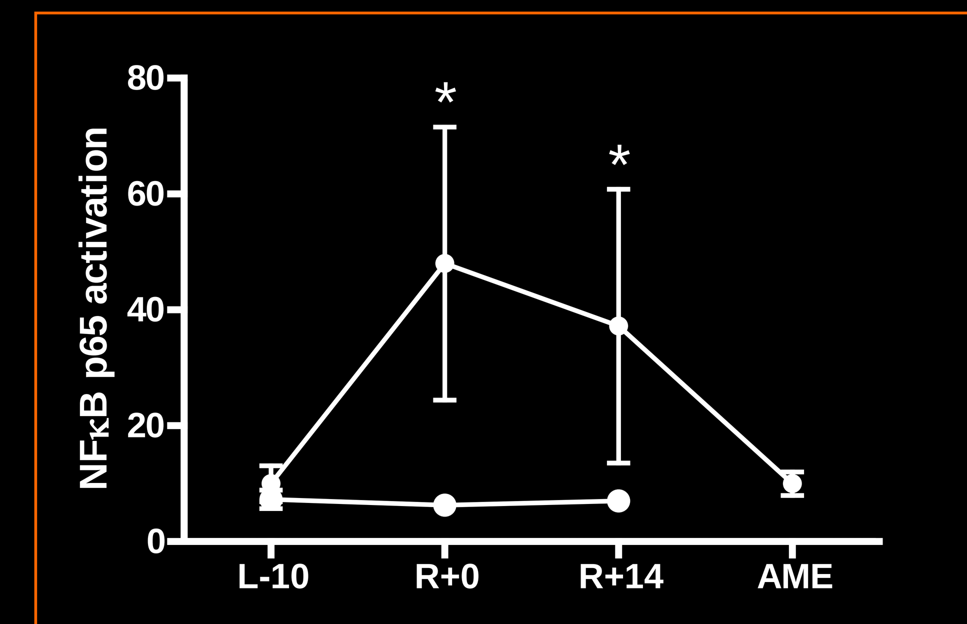


Figure 2. Expression of NF-kB p65 in peripheral blood mononuclear cells of Shuttle crew members (n = 10, filled circles) and age- and sex-matched nonflight controls (n = 7, open circles) before flight (L–10), 3–4 h after landing (R+0), 14 days after landing (R+14), and 3–4 mo after landing (annual medical exam, AME). *Significant difference ($p < 0.001$) between the flight and control groups at R+0 and R+14 and a significant difference from L–10 for the flight group when a two-way repeated-measures ANOVA was performed (excluding the AME data point). When a one-way repeated-measures ANOVA was performed on the flight data, the R+0 and R+14 time points were both different ($p < 0.001$) from L–10 and AME, and AME was not different from L–10.

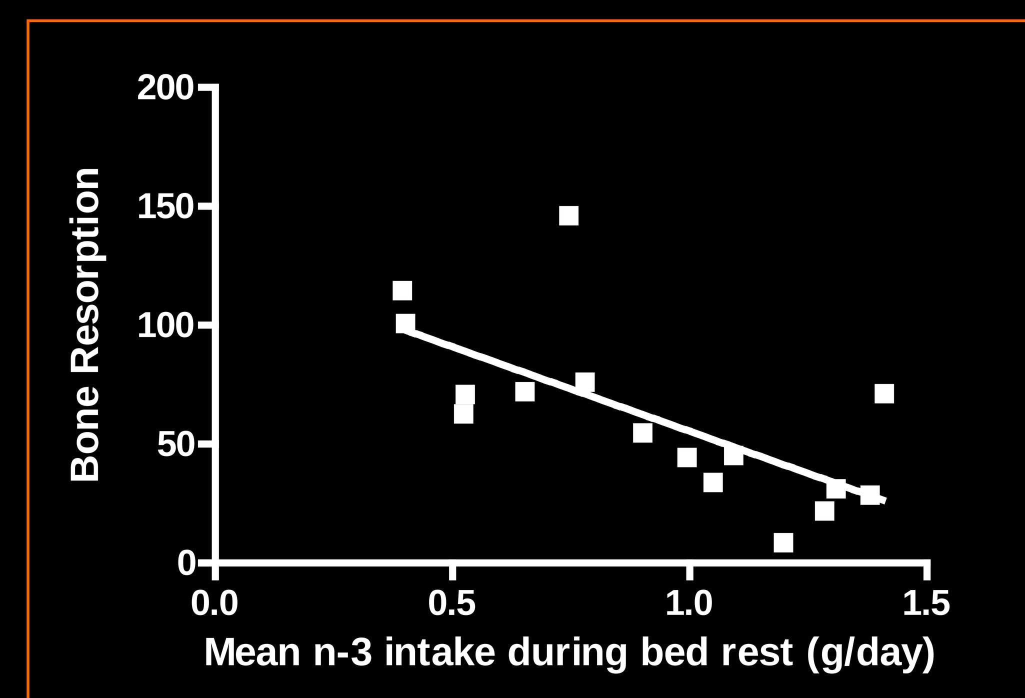


Figure 3. Correlation between the mean daily intake of total omega-3 fatty acids and the percent change in urinary N-telopeptide excretion from pre-bed rest values (n = 16, Pearson $r = –0.62$, $p < 0.01$). The intake of omega-3 fatty acids for each subject is the mean daily intake over the first 60 days of bed rest.

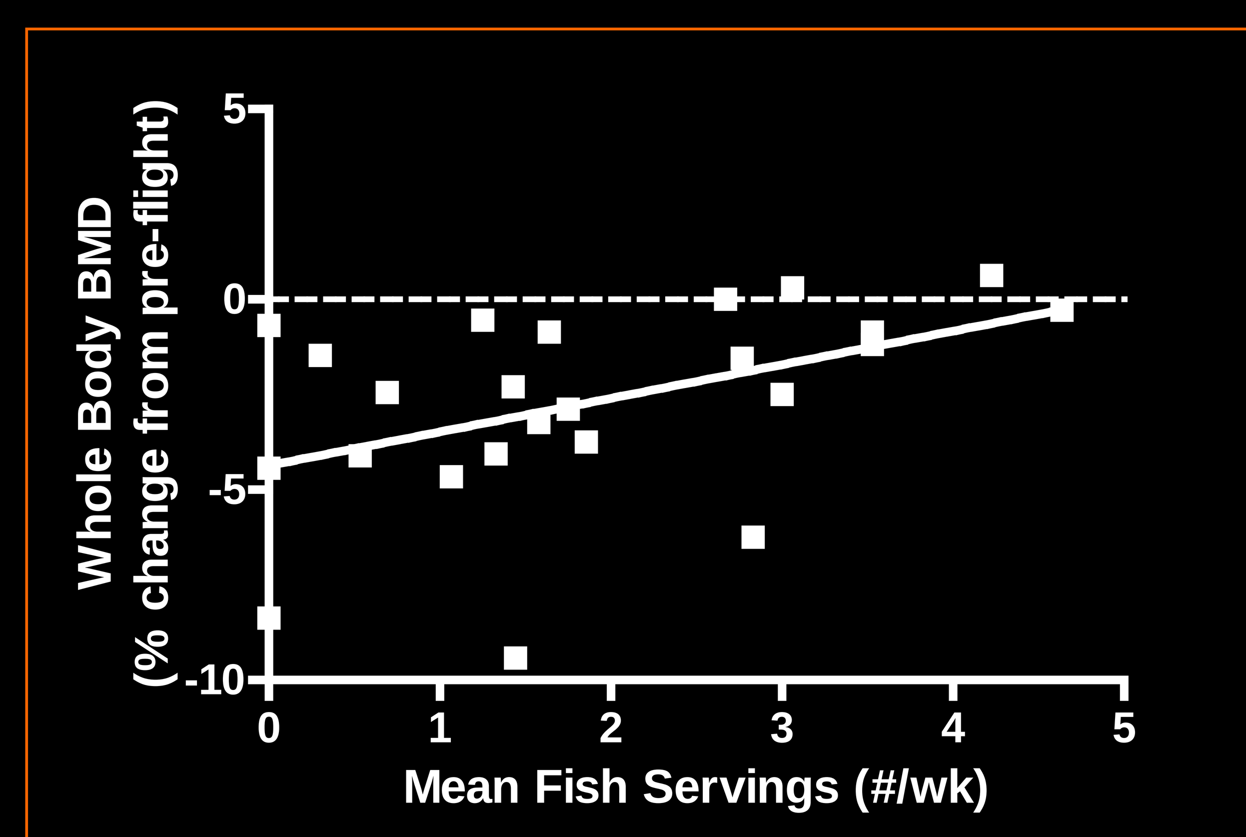


Figure 4. Correlation of the reported intake of fish servings per week during long-duration spaceflight with the percent change in whole-body bone mineral density (BMD) after flight (n = 24, Pearson $r = 0.46$, $p < 0.05$) .

Summary

The results presented here provide evidence that EPA can decrease NF-kB activation by known activators and modeled weightlessness in a HARV, in addition to decreasing osteoclast differentiation. This evidence is supported in the bed rest and spaceflight models, where bone loss is a known health issue. We now have evidence that NF-kB is activated after short-duration spaceflight, and therefore inhibition of NF-kB activation could have many beneficial downstream effects to counteract the negative effects of spaceflight on bone, muscle, and immune function. Beyond muscle, bone, and immune function, the role of n-3 fatty acids in cancer prevention is currently being investigated in animal models of spaceflight radiation effects, with positive results. Thus, there is a good possibility that something as simple as a menu change to increase fish intake might serve as a countermeasure to help mitigate risks related to bone, muscle, immune function, and potentially even radiation. Intervention studies with dietary sources of omega-3 fatty acids are warranted to better understand the mechanism of their action on bone and to determine their effects on other physiological systems (such as muscle and antioxidant defenses). These data will have significant implications for future space exploration, and could benefit the general population.

Reference

- **Zwart S, Pierson D, Mehta S, Gonda S, Smith SM. Capacity of Omega-3 Fatty Acids or Eicosapentaenoic Acid to Counteract Weightlessness-Induced Bone Loss by Inhibiting NF-κB Activation: From Cells to Bed Rest to Astronauts. J Bone Miner Res 25:1049-1057, 2010.**